heavy-chain gene (which flanks the 5′ side of the variable, *V*, region) is properly transcribed only in B cells, even when linked to the SV40 enhancer, which is known to work in many different cell-types. Neuberger suggested that this specificity may be conferred by the conserved sequence that has been found upstream of all immunoglobulin gene *V* regions sequenced to date[6].

The precise role of enhancer sequences in immunoglobulin gene expression has also been brought into question by two observations. First, the λ light-chain gene does not seem to have one, and second the translocations that frequently have juxtaposed immunoglobulin genes with the c-*myc* gene in B-cell malignancies more often than not have removed the enhancer to the reciprocal translocated chromosome (see ref.7 and references therein). The implication of the latter observation is that the immunoglobulin gene enhancer cannot be directly responsible for the deregulation of the c-*myc* gene that is thought to have played a key role in these types of cellular transformation[7].

A similar apparent lack of a requirement for an enhancer is shown by the continued heavy-chain gene expression after spontaneous deletion of regions of the gene that include the enhancer[8,9]. For one of these cases, that of a δ heavy-chain-producing mouse hybridoma cell line[9], Schaffner's group has preliminary evidence that the cloned enhancerless gene must be linked to a new enhancer in order to be expressed when it is reintroduced into B cells. On that basis, Schaffner suggests that enhancers are perhaps required for the establishment of transcription, but are not essential for its maintenance. As Schaffner pointed out, this could account for the apparent lack of requirement for an enhancer for the deregulation of translocated *myc* genes.

If this is so, then why are genes that are turned on by steroid hormones turned off again when the hormone is withdrawn, given that the sequences upstream of genes that confer steroid-responsiveness now seem to be just like the inducible enhancers[10,11]? A possible clue may be in some results reported in Heidelberg by P. Chambon (Institut de Chimie Biologique, Strasbourg).

The principal aim of the experiments reported by Chambon, like those reported by G. Schutz (Institute of Cell and Tumor Biology, Heidelberg) was, however, to answer the puzzle posed in the first sentence of this article — how can one account for the different patterns of expression of steroid-inducible genes in different cell types, all of which contain the appropriate steroid hormone receptors.

For example, the chicken ovalbumin gene is induced by oestrogen in oviduct cells, in which the vitellogenin gene is permanently inactive, whereas in liver cells the ovalbumin gene is permanently inactive and the vitellogenin gene is oestrogen-inducible. Perhaps even more puzzling is the chicken lysozyme gene, which can be induced by oestrogen, progesterone, testosterone or glucocorticoids in oviduct cells, but is permanently inactive in fibroblasts (which contain glucocorticoid receptors) and is expressed constitutively, albeit at a low level, in macrophages.

From an analysis of the expression in cultured cells of microinjected hybrid genes comprising the SV40 T-antigen coding region linked to flanking sequences of the chicken ovalbumin genes (Chambon) or lysozyme genes (Schutz), it seems that, in addition to hormone-responsive sequences, the genes are controlled by other cell-type specific sequences that further restrict their expression. However, in view of the observation of Chambon's group that the ovalbumin flanking sequences allow constitutive gene expression in injected liver cells, the inactivity of the endogenous gene in liver cells remains a puzzle. Chambon suggests the answer may lie in the establishment of domains of permanently inactive and potentially active chromatin during development.

Chambon also reported that hybrid genes containing up to 295 base pairs of the upstream flanking sequences of the ovalbumin gene are constitutively expressed in oviduct and liver cells, but that if 420 base pairs of flanking sequence are used, expression is blocked in oviduct, but not in liver cells. This block can be overcome by steroid hormones or by including an SV40 enhancer element in the microinjected construct. On the basis of these data, Chambon postulates that oviduct cells contain a repressor that recognizes the upstream 'blocking sequence' and keeps the level of expression of the ovalbumin gene minimally low in the absence of hormone. Could it be that such a repressor also has the role of re-establishing a requirement for enhancer-induction following hormone withdrawal?

The notion that enhancers may be required only for the establishment, and not for the maintenance, of a state of transciption is, however, somewhat difficult to reconcile with a model put forward by K. Yamamoto (University of California, San Francisco) to account for some recent results obtained by his group and which may also provide an explanation of some of the remaining puzzles of the regulation of steroid-inducible genes. In essence, Yamamoto reported that pairs of different enhancer sequences in combination can have synergistic effects on the genes to which they are linked, and that these effects depend on the precise nature of the promoter from which transcription of the gene is initiated.

Yamamoto suggests that these observations can be explained if different enhancers stimulate the supply to the promoter of different specific transcription factors, the synergism resulting from a change in the factor that is rate-limiting for transcription in the presence of one or other, or both, the different types of enhancer. Following this line of argument, then, the failure of steroid hormones to increase the low constitutive level of lysozyme gene expression in macrophages could be due to the absence of some other factor which is necessary, though not sufficient, to enhance transcription.

This is all speculation, however, and in truth we still have little idea how even steroid hormone-induced enhancers activate transcription. Even the role of the steroid hormone is still obscure for, as M. Beato (Institut für Physiologische Chemie, Marburg) and W. Schrader (Texas Medical Center, Texas) explained, although the presence of hormone is required for the stimulation of transcription, the hormone-receptors bind quite happily to their specific sequences in the absence of hormone. Hopes that some of this ignorance might soon be dispelled were raised in Heidelberg by Yamamoto's news that his group has cloned cDNAs encoding the rat glucocorticoid receptor. □

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Geoffrey North is an assistant editor of Nature.

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BACTERIOLOGY

AMONG the most striking of the recent rapid advances of science is the development of what we may term bacteriology. While some of this work has been done in this country, by far the greater part has been done abroad, more especially in Germany and France, where its importance is recognised, and where special facilities are afforded by the Governments and various public bodies. In Germany especially, besides the laboratory, supported by the Government, in which Dr Koch works, a number of similar institutions are being established throughout the country; and in France the laboratories of Pasteur and others are established and supported by the Government and by various municipal authorities, every facility for carrying on these researches, and the necessary funds, being provided. In this country, on the other hand, there is no laboratory of the kind, and what work has been done has been by individual investigators working at their own expense and often without suitable accommodation.

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